**SOCIÉTÉ FRANÇAISE DE CHIRURGIE ORALE [FRENCH SOCIETY OF ORAL SURGERY]**

**IN COLLABORATION WITH THE SOCIÉTÉ FRANÇAISE DE CARDIOLOGIE [FRENCH SOCIETY OF CARDIOLOGY] AND THE PERIOPERATIVE HEMOSTASIS INTEREST GROUP**

# Perioperative management of patients treated with antithrombotics in oral surgery.

## RECOMMENDATIONS

**July 2015**

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# Preamble

## Background

Antithrombotic therapy has evolved considerably in recent years with the arrival of new medicinal products. Two new antiplatelet agents, prasugrel and ticagrelor have been used since 2010. Three new oral anticoagulants with selective and specific action on the activated factors II and X, known as direct oral anticoagulants were released: dabigatran in 2008, rivaroxaban in 2009 and apixaban in 2012. For each of these compounds, therapeutic progress is advanced: greater efficacy for new antiplatelet agents with a reduced number of non-responders, the existence of a broad therapeutic range and the absence of biological monitoring for new anticoagulants. However, there is currently no specific antidote on the market for these new anticoagulants.

Finally, more and more patients receive antithrombotic combination therapy (combination of two antiplatelet agents or a combination of an antiplatelet agent and an oral anticoagulant).

The arrival of these new compounds and new protocols for the management and prevention of thromboembolic events led to rethinking the approach of the patient treated with antithrombotics in oral surgery. That is why, in 2013, the Société Française de Chirurgie Orale initiated an update of these recommendations concerning the management of patients receiving therapy with an antiplatelet and/or anticoagulant in oral surgery (SFMbCb Recommendations 2005, 2006).

## Objectives of these recommendations:

1) to define, for each of the families of antithrombotics, the risk of bleeding in the event of maintaining antithrombotic therapy for the different procedures and/or oral surgery invasive procedures;
2) to formalize the perioperative management of patients treated with antithrombotics in case of oral surgery.

## Graduation scale

| Recommendation grades | |
|---|---|
| **A** | **Established scientific evidence**<br>Based on studies with a high level of evidence (Level of Evidence 1): properly designed randomized controlled trials and free of major bias or meta-analyses of randomized controlled trials, decision analyses based on properly conducted studies. |
| **B** | **Scientific presumption**<br>Based on a scientific presumption provided by intermediate level of evidence studies (Level of Evidence 2), such as low level randomized controlled trials, properly conducted non-randomized controlled studies, cohort studies. |
| **C** | **Low level of evidence**<br>Based on lower level of evidence studies, such as case-control studies (Level of Evidence 3), retrospective studies, case series, comparative studies involving significant bias (Level of Evidence 4). |
| **EO** | **Expert opinion**<br>In the absence of studies, the recommendations are based on consensus between the Working Group experts, after consulting with the Peer Review Group. The absence of grading does not mean that the recommendations are not relevant and useful. It should, however, encourage additional studies |

## Abbreviations

| | |
|---|---|
| ACS | Acute coronary syndrome(s) |
| Afib | Atrial Fibrillation |
| APA | Antiplatelet agent(s) |
| aPTT | Activated partial thromboplastin time |
| CVA | Cerebrovascular accident |
| DOA | Direct oral anticoagulant(s) |
| DVT | Deep vein thrombosis |
| HIT | Heparin-induced thrombocytopenia |
| INR | International normalized ratio |
| LMWH | Low-molecular-weight heparin(s) |
| MA | Marketing Authorization |
| MI | Myocardial infarction |
| NSAIDs | Non-steroidal anti-inflammatory drugs |
| PCI | Percutaneous Coronary Intervention(s) |
| PE | Pulmonary embolism |
| UFH | Unfractionated heparin(s) |
| VKA | Vitamin K antagonsits or antivitamin K |
| VTE | Venous thromboembolism |

# Recommendations

## General information for all the antithrombotics

1. The assessment of the risk of surgical bleeding is the responsibility of the surgeon. This assessment is primarily based on the medical examination and preoperative clinical examination (GRADE B).

2. The clinician prescribing the antithrombotic agent is responsible for the assessment of thrombotic risk. His (her) assessment is essential in case of oral surgery with high risk of bleeding in order to determine the action to be taken with regard to the antithrombotic therapy (maintain, temporary suspension with or without replacement therapy) (AE).

3. In the event of oral surgery with low risk of bleeding such as dental avulsions (GRADE A), periodontal surgical procedures or the placing of dental implants (AE), the continuation of antithrombotic therapy is recommended.

4. Predisposing factors for hemorrhagic accidents in patients receiving antithrombotics are multiple and must lead to increased vigilance without being considered to be contraindications (AE).

5. To limit the risk of bleeding and facilitate the management of potential bleeding complications, it is preferable that the procedures are scheduled in the morning and early in the week. In case of multiple surgeries, segmental approach reduces this risk (AE).

6. The management of patients treated with antithrombotics can be done in general practice, subject to the patient's cooperation and the proximity of a health facility (< 50 km or < 1 hour) or a pre-established health care network competent in the management of this type of patients (e.g., oral surgery practice) (AE).

7. The local hemostasis techniques are essential and systematically associated with oral surgery procedures (GRADE A).

8. The continuity of care must be absolutely assured. Any patient treated with antithrombotic agent(s) with postoperative bleeding complications must contact a practitioner who is competent in the management of this type of complication in the context of a care network or optionally a Hospital Dentistry Unit, Oral Surgery, Oral Medicine and/or Maxillofacial Surgery on call (AE).

**9.** In the event of surgery with high risk of bleeding (see Appendix 2), the opinion of the physician who prescribes the antithrombotic agent is essential to assess the risk of thrombosis. In the event of low risk of thrombosis, temporary discontinuation of antithrombotic treatment and management in general practice can be discussed. In the event of high risk of thrombosis, hospital care is recommended (AE).

**10.** In the event of uncontrollable postoperative bleeding by mechanical compression, the rule is the surgical revision of the hemostasis. After local anesthesia, curettage of the clot or a simple clot removal by suction, the surgical wound is revised, then the local hemostasis resumed according to the usual procedures. Postoperative recommendations are renewed. In the event of persistent bleeding despite the resumption of hemostasis, the patient must be hospitalized until the situation is under control (GRADE A).

## Specificities regarding the management of a patient treated with APA

**11.** The continuation of monotherapy with antiplatelet agents (APAs) is recommended for any oral surgery procedure regardless of the associated risk of bleeding (Grade A for dental avulsions and AE for dental implant placement and all other procedures).

**12.** The continuation of a dual therapy with APAs is recommended in case of oral surgery with low risk of bleeding (Grade B for dental avulsions and AE for implant placement and all other procedures). In case of oral surgery with a high risk of bleeding (see Appendix 2), the opinion of the prescribing physician is required in order to determine the optimal therapeutic strategy (AE).

**13.** To date, there is no laboratory examination predictive of the risk of surgical bleeding associated with APAs (GRADE A).

## Specificities regarding the management of a patient treated with VKAs

**14.** Continued treatment with vitamin K antagonists (VKAs) is recommended in case of oral surgery with low risk of bleeding (GRADE A for dental avulsions, GRADE B for implant placement and AE for all other procedures). The INR value should be measured ideally within 24 hours, and within a maximum of 72 hours of surgery. It must be stable and less than 4 (GRADE A). In case of overdose (INR greater than or equal to 4) or unstable INR, surgery should be postponed and the prescribing physician informed. Corrective measures must be initiated immediately by the prescribing physician to bring the INR within the therapeutic range.

**15.** In case of oral surgery with a high risk of bleeding (see Appendix 2), the prescribing physician's opinion is essential in order to assess the risk of thrombosis. In case of low risk of thrombosis, a therapeutic window of 48-72 hours may be proposed by the prescribing physician. VKAs must be discontinued 24-48 hours prior to surgery (24 hours for acenocoumarol and 48 hours for coumadin or fluindione), the INR controlled preoperatively with a target value less than or equal to 1.5 and VKAs should be resumed as soon as possible, at the latest within 24-48 hours after surgery (GRADE C). In the rare case of surgery with a high risk of bleeding in a patient with a high risk of thrombosis, the initiation of a pre- and postoperative relay VKA treatment with heparin (low molecular weight or unfractionated heparin) at a curative dose is possible in hospitals but must remain exceptional (GRADE C).

**16.** Pre and post operative drug prescriptions can lead to drug interactions with VKAs. To control pain, paracetamol and opiates may be prescribed. Aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) are contraindicated because they expose the patient to an increased risk of bleeding when combined with VKAs (GRADE A). To control this risk of infection, sporadic cases of elevated INR have been reported after taking amoxicillin alone or in combination with clavulanic acid, clindamycin, metronidazole, all macrolide antibiotics except spiramycin. The patients must be informed and it is recommended to monitor INR in the days following the prescription (GRADE C). Note that antibiotic prophylaxis (2 g of amoxicillin or 600 mg of clindamycin, 1 hour before surgery) does not change the INR value.

## Specificities of the management of a patient treated with DOAs

**17.** Continued treatment with direct oral anticoagulants (DOA) is recommended in case of oral surgery with low risk of bleeding: dental avulsions, implant placements and for all other procedures (AE).

**18.** In case of oral surgery with a high risk of bleeding (see Appendix 2), the prescribing physician's opinion is essential in order to assess the risk of thrombosis. In case of low risk of thrombosis, DOAs can be stopped by the physician the day before surgery and resumed the day after surgery (therapeutic window of 48 hours) (AE). In the rare case of surgery with a high risk of bleeding in a patient with a high risk of thrombosis, a prolonged discontinuation of treatment with DOA with a relay heparin (low molecular weight heparin or unfractionated heparin) in hospitals is possible, but must remain exceptional (AE).

**19.** To date, there is no laboratory examination predictive of the risk of surgical bleeding associated with DOAs (GRADE A).

**20.** The prescription of clarithromycin for patients treated with DOAs should be avoided (GRADE C).

## Specificities of the management of a patient treated with heparin

**21.** Continued treatment with heparin (low molecular weight heparin or unfractionated heparin) is recommended in case of oral surgery with a low risk of bleeding (GRADE C for dental avulsions, AE for implant placement and all other procedures).

**22.** In case of oral surgery with a high risk of bleeding (see Appendix 2) heparins may be discontinued by the prescribing physician before the procedure (6-8 hours before surgery for unfractionated heparins and 24 hours before for the low molecular weight heparins) in order to limit the risk of perioperative bleeding (GRADE C).

**23.** In case of preoperative discontinuation of heparin therapy, preoperative prescription of activated partial thromboplastin time (aPTT) or of an anti-Xa activity is not necessary (GRADE A).

# APPENDICES

**Appendix 1: Antithrombotic agents (antiplatelet agents and anticoagulants) currently marketed in France in 2015**

| **Antiplatelet agents** | | |
|---|---|---|
| Oral route | | Indications (MA) |
| COX-1 inhibitors | • *Reversible inhibitor*<br>- flurbiprofen (CEBUTID®) | -Secondary preventive treatment following MI after de-obstruction (thrombolysis or transluminal angioplasty) in patients for whom aspirin therapy is temporarily contraindicated (e.g., elective surgery). The medical service rendered in this indication is insufficient. |
| | • *Irreversible inhibitor*<br>- acetylsalicylic acid (ASPIRIN®, KARDEGIC®, ASPIRIN PROTECT®, ASPIRIN UPSA®, CARDIOSOLUPSAN®, PRAVADUAL®) | -Preventive treatment of thromboembolic events associated with atherosclerosis (MI, CVA) |
| $P2Y_{12}$ receptor inhibitors of ADP | • *Reversible inhibitors (thienopyridines)*<br>- ticlopidine (TICLOPIDINE®, TICLID®)<br>- clopidogrel (CLOPIDOGREL®, DUOPLAVIN®, PLAVIX®)<br>- prasugrel (EFIENT®)<br>• *Irreversible inhibitor*<br>- ticagrelor (BRILIQUE®) | -Preventive treatment of thromboembolic events associated with atherosclerosis (MI, CVA)<br>- Chronic arterial insufficiency of the lower extremities<br><br>In combination therapy (aspirin + clopidogrel combination)<br>- ACS without ST segment elevation (unstable angina, Non Q-Wave MI)<br>- MI with ST segment elevation<br>- Patient receiving PCI with stent implantation |
| Phosphodiesterase inhibitors | - dipyridamole (ASASANTINE®, CLERIDIUM®, PERSANTINE®) | -Preventive treatment of CVA after transient or established cerebral ischemic stroke, associated with atherosclerosis, not older than 3 months. |
| Injection | | Indications (MA) |
| GP IIb/IIIa antagonists | - abciximab (REOPRO®)<br>- eptifibatide (INTEGRILIN®)<br>- tirofiban (AGRASTAT®) | - High risk PCI preoperatively |
| Prostacyclin analogue (PGI2) | - iloprost (ILOMEDINE®, VENTAVIS®) | -Treatment of idiopathic pulmonary arterial hypertension in patients in functional Class III |

| **Anticoagulants** | | |
|---|---|---|
| Oral route | | Indications (MA) |
| Vitamin K antagonists<br>(Factors II, VII, IX, X inhibition) | - acenocoumarol (MINI-SINTROM®, SINTROM®)<br>- fluindione ( PREVISCAN® )<br>- warfarin (COUMADIN® ) | - Preventive and curative treatment of VTE<br>Emboligenic heart diseases (prosthetic heart valves, valvulopathy, atrial fibrillation)<br>- Myocardial infarction complicated by heart failure or arrhythmia<br>Recurrent systemic embolism |
| Thrombin inhibitors (anti-IIa) | - dabigatran (PRADAXA®) | - Preventive treatment of systemic embolism in Afib without valvulopathy |
| Activated factor X inhibitors (anti-Xa) | - apixaban (ELIQUIS®) | - Preventive treatment of venous thromboembolic events following orthopedic surgery.<br>- Preventive treatment of systemic embolism in Afib without valvulopathy |
| | - rivaroxaban (XARELTO®) | - Preventive treatment of VTE in orthopedic surgery<br>- Curative treatment of DVT and PE<br>- Preventive treatment of systemic embolism in Afib without valvulopathy |
| Injection | | Indications (MA) |
| Heparins<br>(Factors IIa and Xa inhibitors) | • *Standard or unfractionated heparins (UFH)*<br>- sodium heparin (HEPARIN CHOAY, PANPHARMA®)<br>- calcium heparin (CALCIPARINE®) | - Preventive treatment of arterial and venous thromboembolic events<br>- Curative treatment: VTE, acute coronary syndrome, extracerebral arterial embolism |
| | • *Low molecular weight heparins, subcutaneous route (LMWH)*<br>- dalteparin sodium (FRAGMINE®)<br>- enoxaparin sodium (LOVENOX®)<br>- nadroparin calcium (FRAXIPARINE®, FRAXODI®)<br>- tinzaparin sodium (INNOHEP®) | - Preventive treatment of VTE in surgery and medicine<br>- Curative treatment of DVT and/or PE<br>- Acute coronary syndrome<br>- Renal dialysis in the prevention of clotting in the extracorporeal circuit |
| Other injectable anticoagulants | • *Pentasaccharide*<br>- fondaparinux (ARIXTRA®) | - Preventive treatment of VTE in orthopedic surgery, abdominal surgery in high risk patients (cancer) or in bedridden patients considered to be at high risk<br>- Curative treatment of DVT and/or PE<br>- Acute coronary syndrome |
| | • *Heparinoids*<br>- danaparoid (ORGARAN®) | - Preventive and curative treatment of arterial and venous thromboembolic events in patients with a history or with type II HIT |
| | • *Recombinant hirudins*<br>- bivalirudin (ANGIOX®) | - Anticoagulants in patients undergoing PCI preoperatively |
| | - desirudin (REVASC®) | - Preventive treatment of DVT after orthopedic surgery |
| | - lepirudin (REFLUDAN®) | - Curative treatment of arterial and venous thromboembolic events in patients with a history or with type II HIT |

**<u>Appendix 2</u>: Stratification of the risk of bleeding based on the type of surgery and preventive measures.**

| Types of surgeries and invasive procedures | Preventive measures for bleeding complications |
|---|---|
| **Procedures with no risk of bleeding** | |
| ● Local anesthesia<br>● Descaling | - Simple mechanical pressure hemostasis |
| **Surgeries and procedures with low risk of bleeding**<br>(Surgeries for which externalized bleeding is easily controlled by conventional surgical hemostasis*) | |
| ● Simple avulsion<br>● Multiple avulsions in the same quadrant<br>● Endodontic and periapical surgery (lesion ≤ 2 cm)<br>● Muco-gingival surgery<br>(besides gingival graft with palatine sampling)<br>● Pre-orthodontic surgery of impacted tooth, included<br>● Single implant<br>● Implant(s) release (healing abutment)<br>●Oral mucosa excisional biopsy (≤ 1 cm) | Oral and descaling hygiene measures<br>- Conventional surgical hemostasis<br>- Tranexamic acid |
| **Surgeries and invasive procedures with a high risk of bleeding**<br>(Surgeries for which significant blood loss and/or platelet transfusions are reported in the literature, procedures with operating time > 1 hour, critical procedures by their location (maxillary sinus, floor of the mouth) and/or difficult to control with conventional surgical hemostasis*). | |
| ● Multiple avulsions in several quadrants<br>● Dental avulsion of impacted teeth<br>● Multiple implants in several quadrants<br>● Sinus lift (crestal approach, lateral approach)<br>● Apposition bone graft (in onlay)<br>● Particulate bone grafting and guided bone regeneration<br>● surgery and soft tissue (sialolithiasis)<br>● Enucleation of cysts and benign tumors (lesion > 2 cm)<br>● Closing an oral sinus communication<br>● Excision of pseudotumors and benign tumors of the oral mucosa (> 1 cm) | - Same preventative measure as for surgery with a low to moderate risk of bleeding<br>- Medicinal products derived from blood, fibrinogen and human thrombin<br>- Mono and bipolar electrocoagulation<br>- Give preference to minimally invasive surgeries (flapless and guided implant surgery, sinus crestal approach, etc.)<br>- Preoperative 3D imaging (sinus, symphyseal region) in case of implant placement |
| **Procedures not recommended** | |
| ● Inferior alveolar nerve block: not recommended<br>• Autologous graft: not recommended due to an additional collection site, give preference to heterologous and synthetic grafts | |

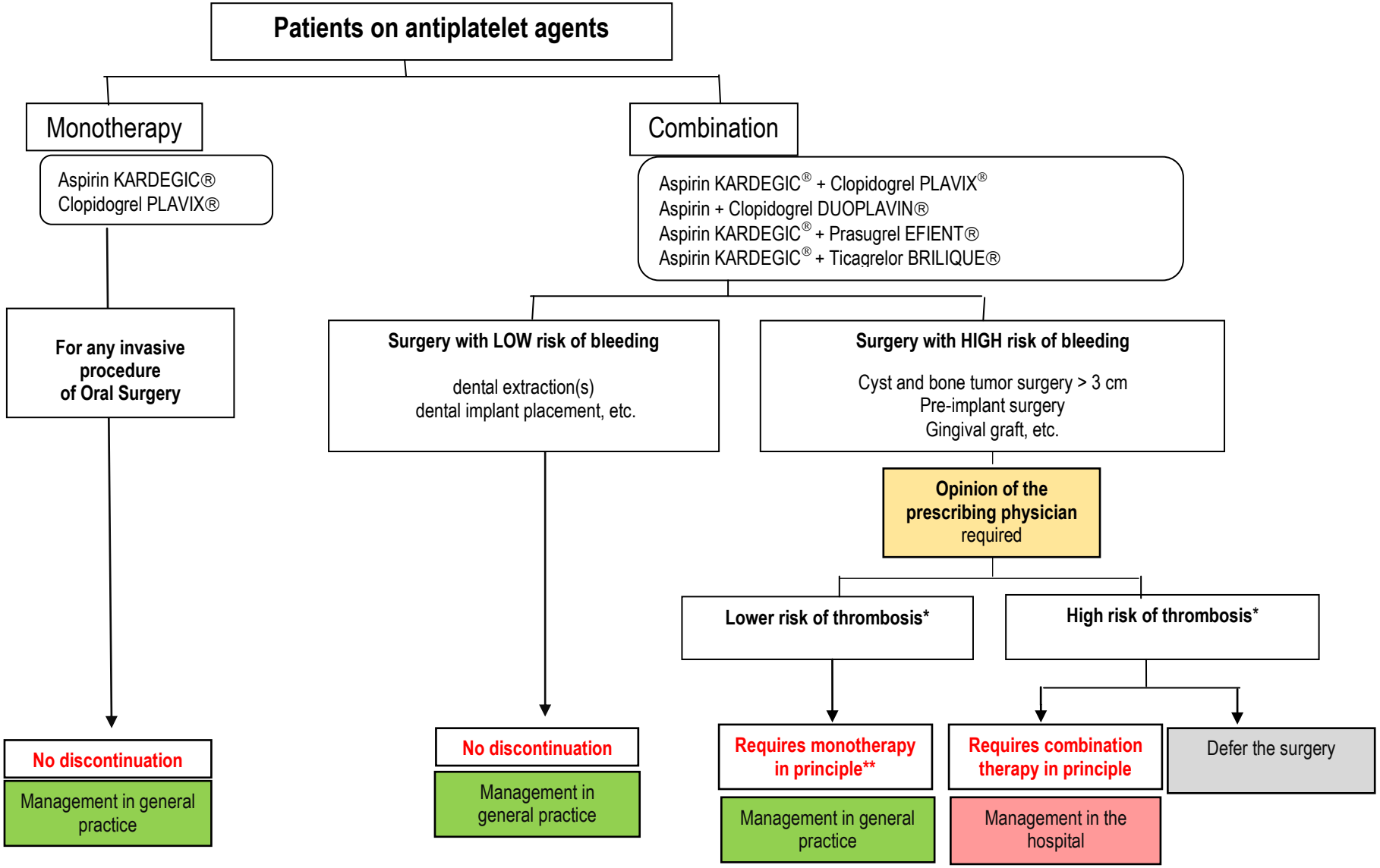
| Contraindicated procedures |
| --- |
| ● All procedures contraindicated in case of an associated risk of infective endocarditis<br>● All procedures with a risk of bleeding in the case where the technical equipment available to the surgeon is inadequate<br>● Bilateral inferior alveolar nerve block: risk of bilateral lateral pharyngeal hematoma and dyspnea<br>● Symphyseal sampling: risk of hematoma of the floor of the mouth and dyspnea<br>● Gingival graft with palatine sampling: risk of injury to the palatine artery |

* **conventional surgical hemostasis**: mechanical hemostasis (pressure + sutures) ± local absorbable hemostatic (collagen or gelatin sponge, cellulose gauze) ± synthetic glue (cyanoacrylate glue).

**Factors that increase the risk of surgical bleeding**: mucoperiosteal detachment beyond the mucogingival line, lingual detachment, avulsion(s) in the inflammation zone, diminished periodontium, duration of surgery > 1 hour (significant blood loss),

**Critical locations**: floor of the mouth, chin symphysis, maxillary sinus

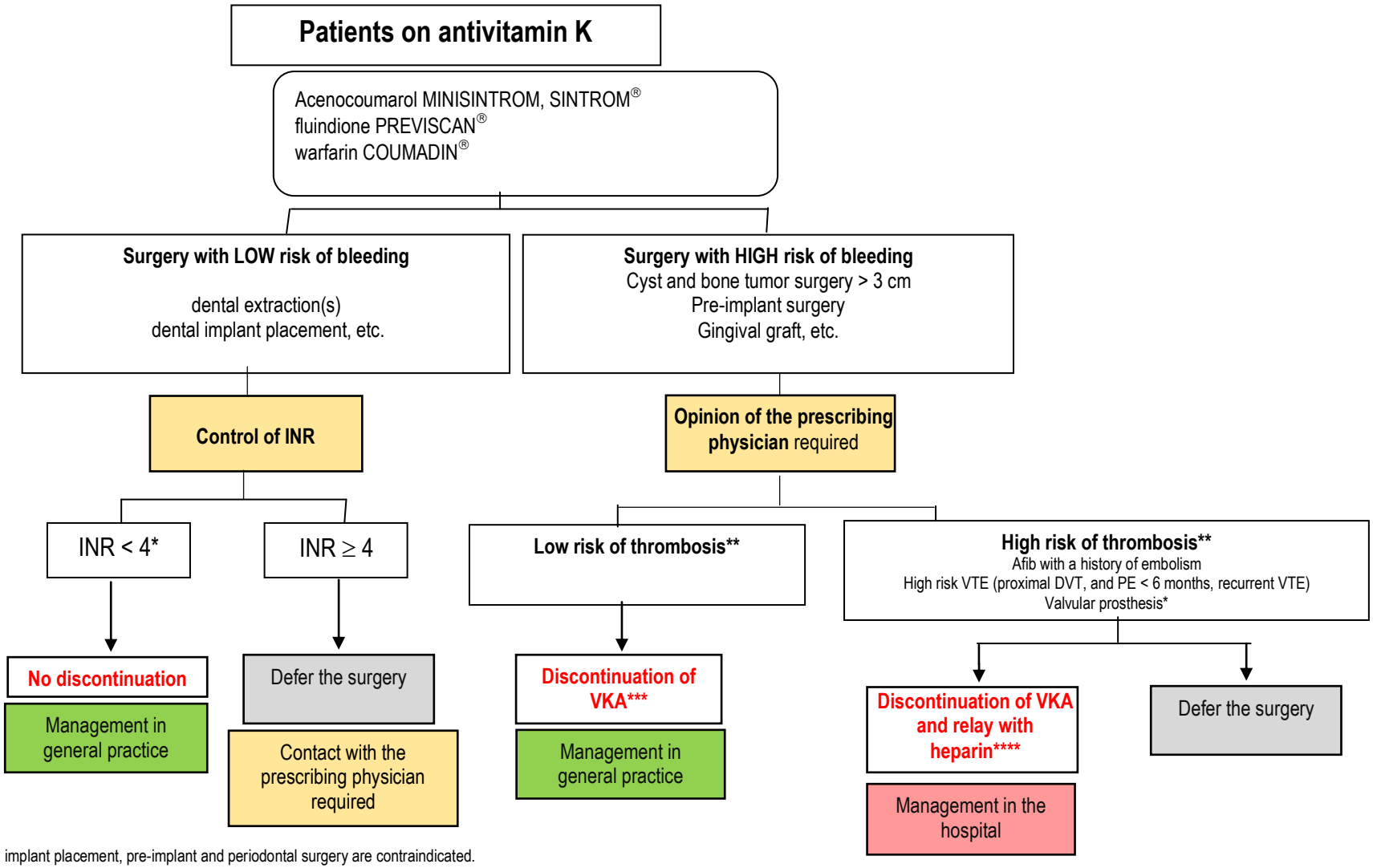
**Appendix 3**: **Systematic algorithm of the management of patients on antiplatelet agents (APAs) during oral surgery.**




* Determining the level of risk of thrombosis available at the website www.has-sante.fr, « Recommandations : Antiagregants-plaquettaires : prise en compte des risques thrombotiques et hémorragique pour les gestes percutanés chez le coronarien » ["Recommendations: Platelet antiaggregants: consideration of risk of thrombosis and bleeding for percutaneous procedures in coronary patients"] (HAS (*Haute Autorité de Santé* [French Health Authority]) in November 2013).

** Monotherapy: continue prescribing aspirin, interruption period: clopidogrel: 5 days, prasugrel: 7 days, ticagrelor 3-5 days.

## Appendix 4: Systematic algorithm of the management of patients on antivitamin K (VKA) during oral surgery.



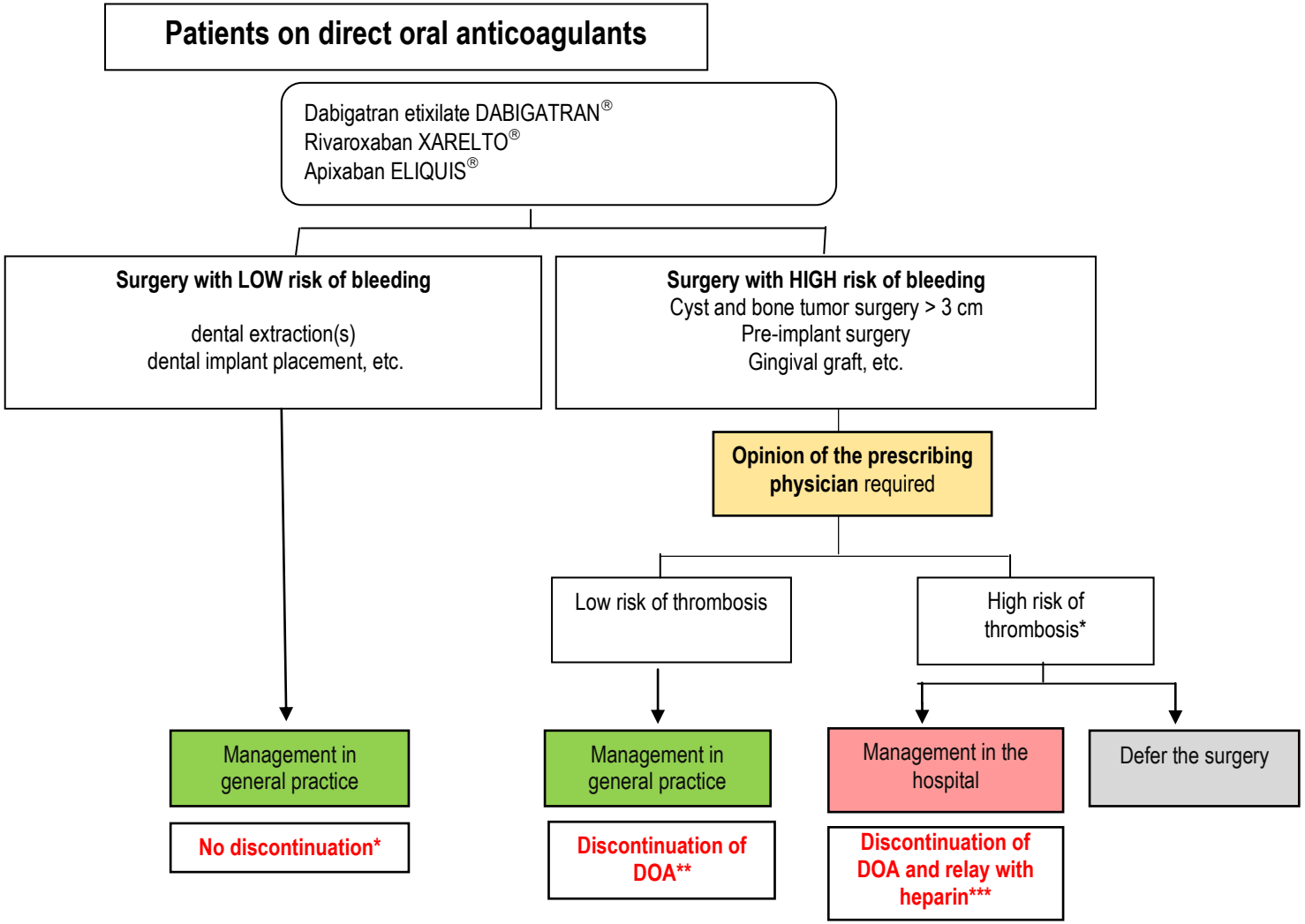

* For patients with valvular prostheses, implant placement, pre-implant and periodontal surgery are contraindicated.

** Determining the level of risk of thrombosis available at the website www.has-sante.fr « Recommandations : Prise en charge des surdosages en antivitamines K, des situations à risque hémorragique et des accidents hémorragiques chez les patients traités par antivitamines K en ville et en milieu hospitalier » ["Recommendations: Management of overdose of vitamin K antagonists, situations at risk of bleeding and bleeding events in patients treated with vitamin K antagonists in general practice and in hospitals"] (GEHT, HAS April 2008).

*** Discontinuation of VKA: Discontinue VKA 4-5 days before the procedure, resumption of VKA in the evening or the day after surgery, perform an INR after 48 hours (HAS 2008)

**** Discontinuation of VKA and relay with heparin: on D-5 discontinuation of VKA, D-3 relay with LMWH (or UFH) with a curative dose, D-1 last injection of LMWH in the morning, UFH in the evening at D0 of the procedure D + 1 resumption VKA and heparin (to be adjusted depending on the risk of bleeding), discontinuation of heparin once the INR target is reached.

**Appendix 5**: **Systematic algorithm of the management of patients on direct oral anticoagulants (DOAs) during oral surgery.**

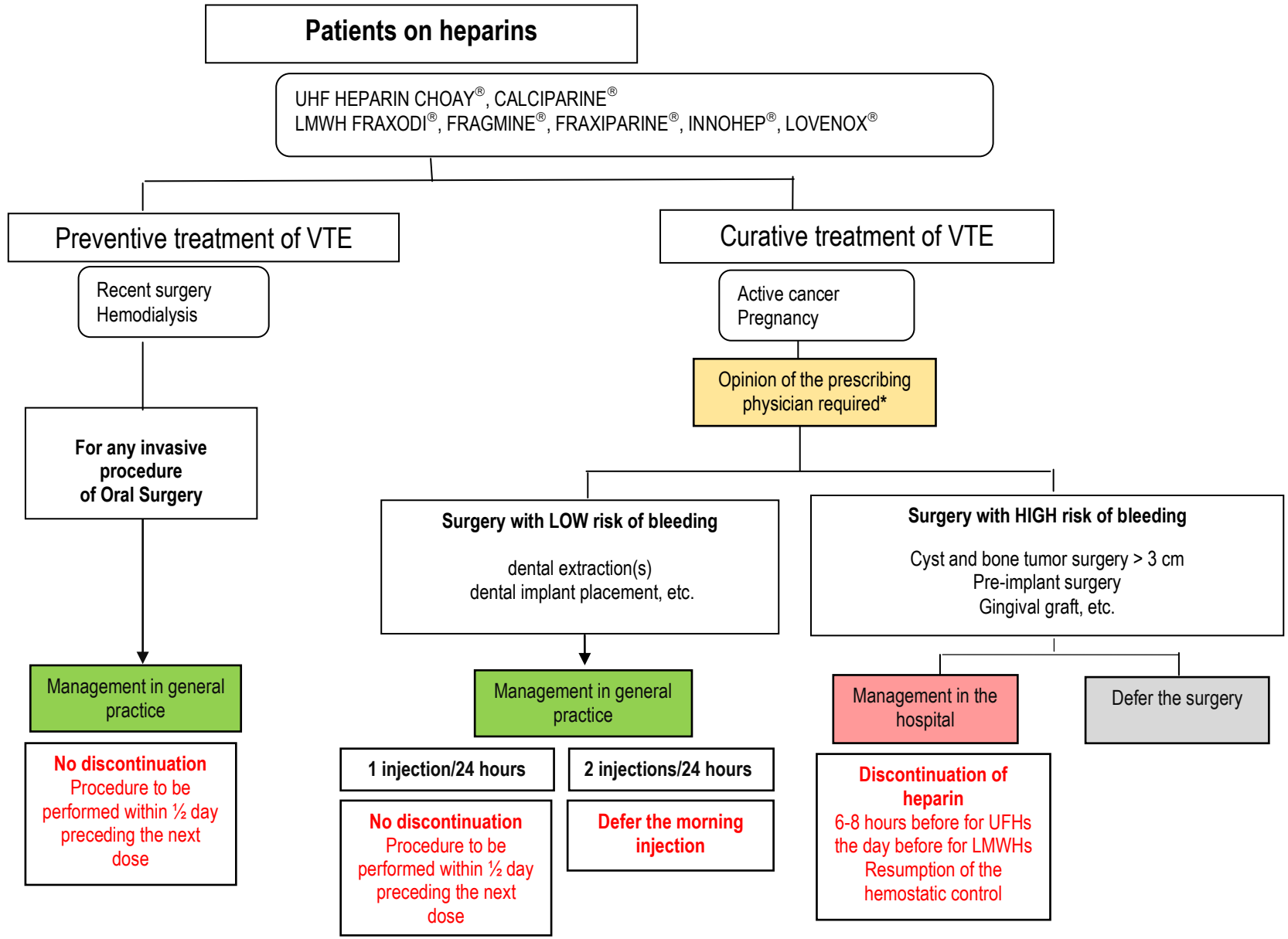



*** No discontinuation**: it is important to specify the age, indication (curative regimen or prevention in orthopedic surgery), the dose and number of doses per day, the time of the last dose, procedure to be performed within the half day preceding the next dose

**** Discontinuation of DOA**: Discontinue DOA on the day before and on the day of the procedure (therapeutic window of 48 hours).

***** Discontinuation of DOA and relay with heparin**: Discontinuation of DOA 5 days before surgery.

**Appendix 6**: **Systematic algorithm of the management of patients on heparins during oral surgery.**




*** check whether there are no other risks and precautions.**